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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/564,829	01/13/2006	David W. Old	(17710)AP	3665

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EXAMINER	
GALLIS, DAVID E	
ART UNIT	**PAPER NUMBER**
1625	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/564,829	OLD ET AL.	
	Examiner	Art Unit	
	David E. Gallis	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Amendment, 37 CFR 1.132 affidavit, and response filed July 6, 2007, and Applicant's summary of the July 30, 2007 interview filed August 31, 2007 have been entered and carefully considered. Receipt of the reference *Kass et al., Arch Ophthalmol, 2002, 120, 701-713* is acknowledged and herein made part the prosecution record.

2. Claims 1, 6, 9, and 10 are amended. Claims 1 through 10 are pending.

3. The rejection of claim 9 under 35 USC 112 first paragraph as failing to comply with the enablement requirement is maintained for reason of record.

As clearly delineated in the previous office action, experimental results that would enable determination of an effective amount of the claimed prostaglandin analog are referred to in the specification but not included in the specification. Page 23, lines 5 and 6 refers to compounds of Table 1 which may be tested for biological activity, even though no such table is present in any part the instant application. Applicant has provide an affidavit by Wha-Bin Im, Ph.D. that includes tabular results supporting enablement of subject compounds as EP4 agonist. However, the procedure for acquiring the data presented clearly indicates that the experimentation involved EP2 receptors rather than EP4 receptors.

Also delineated in the previous office action, the specification, while being enabling for treatment of glaucoma and intraocular hypertension, does not reasonably provide enablement for preventing those conditions. Applicant has provided a reference by Kass et al. that teaches prevention of the onset of primary open angle glaucoma

(POAG), however limited to a population consisting of "individuals with elevated IOP (intraocular pressure)". This prevention of POAG in the cited candidate population does not extrapolate to all individuals. The rejection of claim 9 on the basis of enablement for prevention can be overcome by amending the claim to claim prevention of glaucoma in individuals with elevated IOP.

4. The rejection of claims 6 and 10 under 35 USC 112 second paragraph as being indefinite due to ambiguities in "alteration(s)" of the ω chain structure is maintained for reason of record. Applicant's arguments for the proper interpretation of "alteration" are not found persuasive.

5. As clearly delineated in the previous office action, the said "alteration(s)" of the structure recited in claims 6 and 10, item (a.) encompass "adding, removing, or substituting a non-hydrogen atom of the ω chain". This alteration is far too ambiguous to interpret, since substituting atoms in the ω chain structure can potentially eliminate the chain or eliminate significant substituents and carry into a completely different class of compounds. While page 13 of the disclosure does expand and illustrate "alteration", there is not enough information to characterize the limitations recited in claims 6 and 10. For example, should any non-hydrogen atom be replaced by hydrogen, then whole portions of the ω chain would be eliminated if not the ω chain in its entirety. Also, while the disclosure clarifies that removing an atom includes " any required hydrogen atoms", it does not account for other atoms attached to the eliminated non-hydrogen atom. This must be addressed for the carbon atom bearing the O (or OH) in the ω chain. Elimination of that carbon atom would also eliminate the O (or OH). It is suggested that

Applicant describe the "removing" of a non-hydrogen atom in terms of substituting a non-hydrogen atom with a bond. It is also suggested that Applicant clearly specify what atoms can not be used as "substitutes" in the ω chain, and what atoms can or cannot be "added" to the ω chain. Applicant is hereby advised that if these claimed "alterations" produce compound structures outside the scope of the current examination, a restriction of the subject matter will be required.

6. The rejection of claims 2, 3, 4, 7, and 8 under 35 USC 112 second paragraph, as being indefinite due to lack of antecedent basis is hereby withdrawn.

Applicant has amended claim 1 to include hydrogen as an R substituent, and thereby providing an antecedent basis for the referenced compound.

7. The rejection of claims 6 and 10 under 35 USC 112 second paragraph, as being indefinite due to ambiguities in the referencing of the ω chain is hereby withdrawn.

Applicant has amended claims 6 and 10 to included a clearly defined and annotated "ω chain" as part of the compound structure.

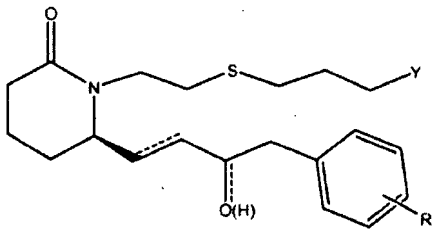
Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

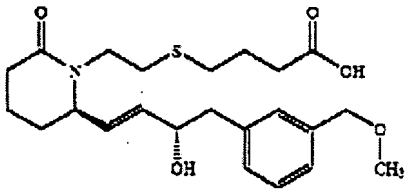
> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

9. Claims 1 through 5 and 7 through 9 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by Elworthy (Application No. 10/754117, file Jan 8, 2004, Pub. No. US 2004/0142969 A1).

Claims 1, 5, and 9 are drawn to a compound comprising the structure below,



Wherein R can be selected to be C_1-C_4 alkyl and Y can be selected to be $-CO_2H$. Elworthy teaches the same structural selection with the compound below. The phenyl



substituent of the Elworthy structure is a substituted C_1 alkyl group (R) of the instant claims 1, 5, and 9, and therefore clearly anticipates these claims.

Claims 2, 3, 4, 7, and 8 are rejected due to their dependency on claims 1, 5, and 9. If written in independent form claims 2, 3, 4, 7, and 8 will overcome the 35 U.S.C. 102(e) rejection above.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 3, 6, 7, 9, and 10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making salts and esters of the claimed compounds, does not reasonably provide enablement for making and determining prodrugs of the claimed compounds. The claims contain subject matter, which was not described in the specification in such a way as to enable one skilled in the art of medicinal chemistry to use the invention.

"The factors to be considered [in making an enablement rejection] have been summarized as a) the quantity of experimentation necessary, b) the amount of direction or guidance presented, c) the presence or absence of working examples, d) the nature of the invention, e) the state of the prior art, f) the relative skill of those in that art, g) the predictability or unpredictability of the art, h) and the breadth of the claims", In re Rainer, 146 USPQ 218 (1965); In re Colianni, 195 USPQ 150, Ex parte Formal, 230 USPQ 546. a) Finding a prodrug is an empirical exercise. Predicting if a certain ester of a claimed alcohol, for example, is in fact a prodrug, that produces the active compound metabolically, at a therapeutic concentration and at a useful rate is filled with experimental uncertainty. Although attempts have been made to predict drug metabolism de novo, this is still an experimental science. For a compound to be a prodrug, it must meet three tests. It must itself be biologically inactive. It must be metabolized to a second substance in a human at a rate and to an extent to produce that second substance at a physiologically meaningful concentration. Thirdly, that second substance must be clinically effective. Determining whether a particular compound meets these three criteria in a clinical trial setting requires a large quantity of

experimentation. b) The direction concerning the prodrugs is found in the disclosure on pages 11 and 12. c) There is no working example of a prodrug of the instant compound genus demonstrating binding and functional data for EP4 receptors (note that the 1.132 affidavit experimentally describes EP2 receptors). d) The nature of the invention is clinical use of compounds and the pharmacokinetic behavior of substances in the body of a mammal. e) The state of the prodrug art currently lacks any standard pharmacokinetic protocol and extensive development must be undertaken to find a prodrug. f) Artisans making Applicants' prodrugs would require a Ph. D. degree and several years of industrial experience. g) It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. See In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). h) The breadth of the claims includes all of the hundreds of compounds of the formula depicted and specified in claim 1 as well as the presently unknown list of potential prodrug derivatives thereof embraced by claim 1.

11. Since this Office Action contains a 35 USC 102(e) and 112 first paragraph rejections based on the continued examination of previously presented subject matter **THIS ACTION IS NON-FINAL.**

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David E. Gallis whose telephone number is 571-272-9068. The examiner can normally be reached on Mon-Fri 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-1600. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

David E. Gallis
Patent Examiner

BERNARD DENTZ
PRIMARY EXAMINER